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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,387	06/07/2001	David S. Jones	252312007500	2401

25226 7590 02/25/2003

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EXAMINER
AUDET, MAURY A

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/877,387	Applicant(s) JONES, DAVID S.	
	Examiner Maury Audet	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *2-16 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,17-19 and 21-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7, 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Change of Art Unit Designation

1. Please note: The Art Unit location of this application in the PTO has changed from Art Unit 1635 to Art Unit 1654. To aid in matching papers in this application, all further correspondence regarding this application should be directed to **Group Art Unit 1654**.

Election/Restrictions

2. Applicant's election *without* traverse of Group III, claims 1, 17-19, ~~24~~ 21-34, in Paper No. 13 is acknowledged.

Status of the Claims

3. Claims 1-34 were originally filed in the present application. Claims 2-16, and 20 are withdrawn from further consideration as being drawn to non-elected inventions in Paper No. 13. Claims 1, 17-19, and 21-34 are pending in the present application and examined on the merits.

Domestic Priority

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e), to U.S. provisional Application No. 60/210,439, filed June 8, 2000, is acknowledged.

Information Disclosure Statement

5. The Information Disclosure Statement filed 1/11/02 and the Supplemental Information Disclosure Statement filed 8/14/02 have been considered. In accordance with MPEP § 609, initialed copies of the respective Form PTO-1449 are attached hereto.

Objections

6. The following claims are objected to:

Claim 18 is objected to on the grounds of singular versus plural grammatical confusion (i.e. molecule (singular), followed by group (plural species).

Claim 34 is objected to on the grounds that the 'O' in NO requires capitalization.

Appropriate correction of the above is required.

Rejections

35 U.S.C. § 112, 2nd ¶

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "high" in claim 1 is a relative term which renders the claim indefinite. The term "high" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of "high" (namely the range, upper and lower limits of the PEO group), and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant is asked to specifically claim the 'high' 'range', within the scope of the specification, or provide a reference indicating what those skilled in the art have determined to constitute a 'high' molecular weight polyethylene oxide group.

The term "analog" in claims 21 and 23 is indefinite, because the claims and the specification do not describe the metes and bounds of what is included as an "analog", and one

of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant is asked to amend the claims by removing the term 'analog' or specifically claim those polypeptide and αGal epitope embodiments, within the scope of the specification, contemplated as analogs.

35 U.S.C. § 112, 1st ¶

8. Claims 21 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Namely, the 'analogs' of polypeptide and αGal epitope embodiments (rejected supra under § 112 2nd ¶), have not been described in such a manner that it can be determined precisely what applicant possesses as 'analogs' respectively.

35 U.S.C. § 103 Obviousness

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 17-19, and 21-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over IVERSON et al. (Iverson et al.) in view of LANZA et al. (Patent No. 6,368,612 B, issued April 9, 2002, hereafter Lanza et al.).

The claimed invention is drawn to a chemically defined valency platform molecule comprising at least one high molecular weight polyethylene oxide (cl. 1); further comprising a biologically active molecule (cl. 17) (selected from poly(saccharides), poly(amino acids), nucleic

acid and lipids (cl. 18); is a β2GPI domain 1 polypeptide or analog (cl. 21); or αGal epitope or analog that binds to an anti-αGal antibody (cl. 23)); further comprising (as a pharmaceutically acceptable composition) a carrier (cl. 24). The conjugate is further defined as a "B cell toleragen" (cl. 19), and 'effective for the treatment of antibody mediated thrombosis' (cl. 22). The invention is further defined as a conjugate (cl. 25) (selected from compounds 200, 202, 203, 205, or 300, wherein D1 is amino acids No. 2-63 of SEQ ID NO: 2 (cl. 34)); of a chemically defined valency platform molecule (at least 3 aminooxy groups (cl. 26); at least 3 carbamate groups (cl. 27); a core group and at least three arms with respective termini (cl. 29)); and polypeptide comprising a B2GPI domain 1 polypeptide (which can specifically bind to a β2GPI-dependent antiphospholipid antibody (cl. 30); lacks a T cell epitope capable of activating T cells in an individual having B2GI dependent antiphospholipid antibodies (cl. 31); is at least five contiguous amino acids of SEQ ID NO: 2 (cl. 32); is amino acids Nos. 2-63 of SEQ ID NO: 2 (cl. 33)); further comprising at least one high molecular weight polyethylene oxide (a molecular weight greater than 22,000 Daltons (cl. 28).

Iverson et al. teach a 'multivalent platform' (page S168, ¶ 1 under 'Discussion') containing (diaminotri)ethylene glycol (page S167, end of column 1, under 'Toleragen construction'); for covalently linking a biologically active molecule in the broad sense of an 'antibody-binding epitope' (page S166, column 2), such as a 'peptide epitope' (page S166, column 2). Iverson et al. teach a β2GPI domain I polypeptide analog wherein they 'employed β2GPI-dependent anticardiolipin antibodies from a high GPL patient to identify a peptide epitope that specifically bound these antibodies'; and further teach the 'absence of T cell help' indicating that peptide epitope lacked capability of activating T cells(page S166, column 2).

Iverson et al. also teach the conjugate of the platform and peptide epitope with a 'carrier' (abstract). Iverson et al. further teach a multivalent platform therapy that has 'B cell tolerance', for the treatment of 'thrombotic episodes' associated with such diseases as 'antiphospholipid syndrome' (page S168, column 2, ¶ 1, 2). Iverson et al., in structure (B) on page S168, teach a platform with at least three (here four) aminooxy (NO) groups, and a core group and at least three (here four) arms, wherein each arm comprises a terminus. Iverson et al. also teach the use of two carbamate groups (HN-COO), within the single platform structure depicted and discussed. Iverson et al. does not specifically teach polyethylene oxide, αGal epitope, β2GPI domain I polypeptide, *at least 3* carbamate groups (HN-COO), at least five contiguous amino acids or amino acids 2-63 of SEQ ID NO. 2, or compounds 200, 202, 203, 205, and 300.

Lanza et al. teach a therapeutic device, for inhibiting the host immune response in various disease states, that includes 'polyethylene glycol (PEG) (or) polyethylene oxide (PEO) (column 3, lines 23-25) and more specifically, the 'use of a high molecular weight molecule, e.g., a high molecular weight PEO, e.g., of about 1-8 million Da' (column 13, lines 63-65). One of ordinary skill in the art at the time the invention was made would have found it prima facie obvious to use a platform with PEO, with a molecular weight greater than 22,000 Daltons, because Lanza et al. teach the use the interchangeable use of PEG and PEO with a device directed toward the treatment of autoimmune-based diseases. Lanza et al. also teach the use of αGal epitope (column 45, lines 22-29), in the device containing PEO. One of ordinary skill in the art at the time the invention was made would have found it prima facie obvious to use αGal epitope as a biologically active agent, because Lanza et al. teach the use of αGal in the treatment of autoimmune-based diseases, since it was a known site on antigen that antibodies bind to.

Although Iverson et al. does not teach that more than two carbamate groups (specifically three or more) could be chemically bound in the platform, one of ordinary skill in the art at the time the invention was made would have found it prima facie obvious to use more than two (i.e. three or more) carbamate groups, if desired, since there is no teaching that the number of carbamate groups in any way positively or negatively impacts the structure or function of the platform.

Although neither Iverson et al. nor Lanza et al. teach the specific compounds 200, 202, 203, 205, and 300. One of ordinary skill in the art at the time the invention was made would have found it prima facie obvious to make and use the specific structures, since Iverson et al. teach the use of a similar structure (valency platform molecule) employing PEG in autoimmune diseases, and Lanza et al. teach the interchangeable use of PEO and PEG within a device directed toward autoimmune diseases.

Claims 32-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over IVERSON et al. (Iverson et al.) in view of LANZA et al. (Patent No. 6,368,612 B, issued April 9, 2002, hereafter Lanza et al.) further in view of MATSUURA et al. (Patent No. 5,998,223, issued December 7, 1999, hereafter Matsuura et al.).

As discussed supra, Iverson et al. teach the use of a valency platform molecule with ethylene glycol, and β2GPI domain I polypeptide analog. Lanza et al. teach the use of polyethylene oxide with anti-autoimmune biological active molecules (i.e. αGal epitope).in various treatments directed towards autoimmune diseases. Neither Iverson et al. or Lanza et al. teach SEQ ID NO. 2 or five contiguous amino acids therefrom. Matsuura et al. teach the identification, clarification of domain I-V functionality β2GPI polypeptide (including domain I,

amino acids 2-63 of SEQ ID NO. 2, and five contiguous amino acids therefrom), and the necessary use of this polypeptide and various domains in the assay of autoantibody (i.e. anticardiolipin (ACL)) from antiphospholipid patients (column 2, sequence listing). One of ordinary skill in the art at the time the invention was made would have found it prima facie obvious to identify and use domain I (amino acids 2-63 of SEQ ID NO. 2), as well as at least five contiguous amino acids that could functionally bind cardiolipin antibody, because Matsuura clarified the functionality of, among other domains, domain I., in order to bind ACL, and treat, among other symptomology, antibody mediated thrombosis associated with antiphospholipid syndrome.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 703-305-5039. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-1234 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

MA
February 24, 2003

Brenda Brumback
BRENDA BRUMBACK
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